REMARKS/ARGUMENTS

The foregoing amendments in he specification and claims are of formal nature, and do not add new matter.

Prior to the present amendment, Claims 28-47 were pending in this application and were rejected on various grounds. Claims 37 and 42 have been cancelled without prejudice. The rejection of the remaining claims is respectfully traversed.

Specification

The specification has been amended to remove embedded hyperlink and/or other form of browser-executable code.

Priority

According to the Office Action, "this application is supported by the disclosure in International Application Serial No. PCT/US00/04342, filed February 18, 2000 but is not supported by any of the earlier applications because no utility for the claimed polypeptide, PRO 1412, is disclosed in the earlier applications." Applicants rely on the chondrocyte re-differentiation assay (Example 153) for support of patentable utility. This data was first disclosed in International Application Serial No. PCT/US00/04342 filed on February 18, 2000, the priority of which is claimed in the present application.

Claim Objections

Claim 38 is objected because according to the Examiner there are two Claim 38's. Applicant respectfully submit that only one Claim 38, as shown above, was included in the preliminary amendment filed on December 11, 2001. Accordingly, the objection should be withdrawn.

Claim Rejections – 35 U.S.C. §112, Second Paragraph

Claims 28-33, 37, and 41 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner noted that "[t]he limitation that the encoded protein comprises an 'extracellular domain' ... 'lacking its associated signal peptide' (Claim 28,

part (d), for example) is indefinite[.]"

Since the term "extracellular domain ... lacking its associated signal peptide" is no longer present in Claims 28-33 and 41(and, as a consequence, those claims dependent from the same), the rejection is believed to be moot, and should be withdrawn.

Claim 37 has been cancelled without prejudice and hence, the rejection to this claim is believed to be moot, and should be withdrawn.

Claim 42 is rejected as "indefinite," since, according to the Examiner, the term "stringent conditions" is not defined in the specification. Claim 42 has been canceled without prejudice and hence, the rejection is believed to be moot, and should be withdrawn.

Claim Rejections – 35 U.S.C. §112, First Paragraph

Claims 28-32 and 44-47 are rejected under 35 U.S.C. §112, first paragraph, because "the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims." Furthermore, the Examiner has noted that the specification is "enabling for an isolated polypeptide having at least 80% nucleotide sequence identity to the polypeptide encoding SEQ ID NO:139 or the nucleic acid encoding the mature form of the polypeptide, which polypeptide induces proliferation of chondrocyte." (See Office Action, page 3).

Present claim amendments (and, as a consequence, those claims dependent from the same) recite a functional limitation wherein the claimed nucleic acid molecules encode polypeptides "capable of inducing chondrocyte redifferentiation." In addition, Applicants submit that the specification provides ample enablement for such polypeptides based on the *in vitro* data provided in the chondrocyte redifferentiation example (Example 153). Coupled with the general knowledge in the art at the time the invention, Applicants submit that the present application provides sufficient guidance to one skilled in the art to use the invention without undue experimentation. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174* (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01. Hence, the present rejection should be withdrawn.

Claim Rejections – 35 U.S.C. §112, First Paragraph

Claims 28-32 and 44-47 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of sufficient written description. The Examiner noted that in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Present claim amendments (and, as a consequence, those claims dependent from the same) recite a functional limitation wherein the claimed nucleic acid molecules encode polypeptides "capable of inducing chondrocyte redifferentiation." Since the claimed genus is now characterized by a combination of structural and functional features, one skilled in the art at the effective priority date of the present application would be reasonably accepted that the inventors were in the possession of the invention as claimed. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim 43 is rejected under 35 U.S.C. §112, first paragraph, for alleged lack of sufficient written description. Claim 43 is now dependent on amended Claim 41 which recite a functional limitation wherein the claimed nucleic acid molecules encode polypeptides "capable of inducing chondrocyte redifferentiation." Accordingly, one skilled in the art at the effective priority date of the present application would be reasonably accepted that the inventors were in the possession of the invention as claimed. Hence, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

Claim Rejections – 35 U.S.C. §102

Claims 28-32 and 41-47 are rejected under 35 U.S.C. §102(a) as being anticipated by International Patent Application Publication No. WO 00/00610 (Lal *et al.*, publication date January 6, 2000). Applicants respectfully submit the attached Declaration by Dr. Desnoyers, the consideration of which is respectfully requested.

Dr. Desnoyers, along with other inventors of the above-identified application, conceived and reduced to practice the invention claimed in the above-identified application in the United States prior to January 6, 2000.

The polypeptide designated as PRO1412 was first disclosed in the priority document, International Application No. PCT/US99/20111 filed on September 1, 1999. The description of

PRO1412 can be found at least on page 12 of the PCT publication. In addition, the amino acid sequence (SEQ ID NO: 140) and its encoding nucleic acid sequences (SEQ ID NO: 139) for PRO1412 can be found at least on page 302 under the description of Figures 83 and 84 and in the claims of the PCT publication.

For each PRO polypeptide, its encoding nucleic acid sequence is assigned to a DNA number and an UNQ Number. As indicated in the brief description of Figure 83 on page 302 of the PCT publication and on page 289 of the present specification, the assigned numbers for PRO1412 are DNA 64897-1628 and UNQ730.

The attached Exhibits A and B show the positive results obtained for PRO1412 polypeptide based on the chondrocyte proliferation assay. Chondrocyte proliferation assay is used to find agents that are capable of inducing chondrocyte proliferation and/or redifferentiation. The assay was performed on PRO1412 polypeptide following the protocol described in Example 153 of the specification. According to the protocol, isolated chondrocyte cells are seeded in 96 well plates with either serum-free medium (negative control), staurosporin (positive control) or the test PRO polypeptide. After 5 days, fluorescence dye is added to each plate and measured. The readout of the fluorescence from a plate containing the serum-free medium is measured to establish a background fluorescence level. A positive result in the assay is obtained when the fluorescence of the PRO polypeptide-treated sample is more like that of the positive control than the negative control. This type of fluorescence determination, wherein the readout is compared to positive and negative controls, is well known in the art.

The Genengenes database stores experimental data from the chondrocyte proliferation assay for each PRO polypeptide according to its UNQ number. The database additionally assigns a pin number (shown under "LOT Name") for each UNQ number. For PRO1412 polypeptide, the assigned pin number is PIN753-1.

A copy of a page from the Genengenes database displaying the positive results for PRO1412 polypeptide is shown as Exhibit A to the declaration.

Copies of pages from Dr. Desnoyers' laboratory notebook showing the positive results for PRO1412 from the assay are shown as Exhibit B. The positive results shown in Exhibit B for PRO1412 polypeptide, identified by its pin number PIN753-1, are indicated with an arrow.

All of the results shown in Exhibits A and B were obtained prior to January 6, 2000.

The Declaration clearly show that the PRO1412 polypeptide and its encoding nucleic acid were conceived and reduced to practice prior to January 6, 2000. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **39780-2830 P1C48**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: April 7, 2004

By: _____
Ginger R. Dreger (Reg. No. 33,055)

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